Application No.: 10/045,903

Page 2

Claim Listing

- 1. (Canceled)
- 2. (Currently amended) The method of Claim 33 wherein R³ is:
- (a) optionally substituted heterocyclyl;
- (b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO₂R' (where R' is alkyl) or SO₂NR'R" (where R' and R" are independently hydrogen or alkyl);
- (c) heteroalkyl;
- (d) heteroalkenyl;
- (e) heteroalkoxy;
- (f) optionally substituted heterocyclylalkyl or heterocyclyloxy;
- (g) optionally substituted heterocyclylalkenyl;
- (h) optionally substituted heterocyclylalkynyl;
- (i) optionally substituted heterocyclylalkoxy;
- (j) optionally substituted heterocyclylalkylamino;
- (k) optionally substituted heterocyclylalkylcarbonyl;
- -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, -SO₂R¹⁴,
 -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵,
 R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl;
- (m) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
- (n) arylaminoalkylene or heteroarylaminoalkylene; or
- (o) Z-alkylene-NR³⁰R³¹ where Z is -NH-, -N(alkyl)- or -O-, and R³⁰ and R³¹ are independently of each other, hydrogen, alkyl or heteroalkyl, wherein

PATENT

Goldstein et al.

Application No.: 10/045,903

Page 3

said alkylene and alkyl groups are optionally substituted with one to two groups selected from OH and O(alkyl).

- 3. (Original) The method of Claim 2 wherein R¹ and R² are hydrogen; and B is phenyl.
 - 4. (Original) The method of Claim 3 wherein A is phenyl.
- 5. (Original) The method of Claim 4 wherein R⁴ is hydrogen; and R⁵ is halo or alkyl.
- 6. (Original) The method of Claim 5 wherein R⁵ is chloro, fluoro or methyl; and R⁶ is hydrogen, chloro, fluoro, methyl or methoxy.
- 7. (Original) The method of Claim 5, wherein R³ is optionally substituted heteroaryl.
- 8. (Original) The method of Claim 7, wherein R³ is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.
 - 9. (Original) The method of Claim 8, wherein \mathbb{R}^3 is at the 3-position.
 - 10. (Original) The method of Claim 9, wherein R⁵ is 4-F and R⁶ is hydrogen.
- 11. (Original) The method of Claim 9, wherein R⁵ is 2-Me and R⁶ is hydrogen.
- 12. (Original) The method of Claim 5, wherein R³ is optionally substituted phenyl.

Goldstein et al.

PATENT

Application No.: 10/045,903

Page 4

13. (Original) The method of Claim 12, wherein R³ is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.

- 14. (Original) The method of Claim 13, wherein R³ is at the 3-position.
- 15. (Original) The method of Claim 14, wherein R⁵ is 4-F and R⁶ is hydrogen.
- 16. (Currently Amended) The method of Claim 5 wherein R³-is: A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound of Formula (I):

wherein:

R¹ is hydrogen or acyl;

R² is hydrogen or alkyl;

A is an aryl ring;

B is an aryl ring;

 \mathbb{R}^3 is:

- (a) heteroalkyl;
- (ba) heteroalkoxy;
- (eb) optionally substituted heterocyclylalkyl;
- (dc) optionally substituted heterocyclylalkoxy;
- (ed) optionally substituted heterocyclylalkylamino;

PATENT

Goldstein et al.

Application No.: 10/045,903

Page 5

- -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted heteroaryl, -CONR¹²R¹³, SO_2R^{14} , - $SO_2NR^{15}R^{16}$, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl; ΘF
- (f) heteroaryl selected from pyridinyl, N-oxidopyridinyl or pyridonyl; or
- (g) substituted phenyl selected from sulfamoylphenyl,
 methylsulfonylphenyl, carboxyphenyl or ethoxycarbonylphenyl;

	memyisunonyipin	
<u>R⁴ is:</u>		
	(a)	hydrogen;
	(b)	halo;
	(c)	<u>alkyl;</u>

- (d) alkoxy; and
 - (e) hydroxy;

R⁵ is:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) haloalkyl;
- (e) thioalkyl;
- (f) hydroxy;
- (g) amino;
- (h) alkylamino;
- (i) dialkylamino;
- (j) heteroalkyl;
- (k) optionally substituted heterocycle;
- (l) optionally substituted heterocyclylalkyl;
- (m) optionally substituted heterocyclylalkoxy;
- (n) alkylsulfonyl;

Goldstein et al.

Application No.: 10/045,903

 \mathbb{R}^6 is:

Page 6

(o) aminosulfonyl, mono-alkylaminosulfonyl or
dialkylaminosulfonyl;
(p) heteroalkoxy; and
(q) carboxy;

(a) hydrogen;
(b) halo;
(c) alkyl; and

or a prodrug, individual isomer, mixtures of isomers, pharmaceutically acceptable salt or solvate thereof.

17-21. (Canceled)

(d)

alkoxy;

- 22. (Original) The method of Claim 16, wherein R³ is heteroalkoxy.
- 23. (Original) The method of Claim 22, wherein R³ is at the 3-position and is selected from the group consisting of 3-dimethylaminopropoxy, 2-dimethylaminoethoxy, 2-hydroxyethoxy, 2,3-dihydroxypropoxy, and 2,2-(dihydroxymethyl)ethoxy.
- 24. (Original) The method of Claim 23 wherein R⁵ is 4-F or 2-Me and R⁶ is hydrogen.
- 25. (Original) The method of Claim 16, wherein R³ is optionally substituted heterocyclylalkyl, optionally substituted heterocyclylalkoxy or optionally substituted heterocyclylalkylamino.
- 26. (Original) The method of Claim 25, wherein R³ is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxo-pyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl, 4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydroxy-

Goldstein et al.

PATENT

Application No.: 10/045,903

Page 7

piperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.

- 27. (Original) The method of Claim 26 wherein R⁵ is 4-F or 2-Me and R⁶ is hydrogen.
- 28. (Original) The method of Claim 16 wherein R³ is
 -Y-(alkylene)-R⁹ where Y is a single bond, -O- or -NH- and R⁹ is optionally substituted
 heteroaryl, -CONR¹²R¹³, -SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹ where R¹², R¹³,
 R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently of each other hydrogen, alkyl or heteroalkyl.
- 29. (Original) The method of Claim 28, wherein Y is a single bond and R^9 is SO_2R^{14} or $-SO_2NR^{15}R^{16}$.
- 30. (Original) The method of Claim 29 wherein R³ is methylsulfonylethyl or sulfamoylethyl.
- 31. (Original) The method of Claim 30 wherein R⁵ is 4-F or 2-Me and R⁶ is hydrogen.
 - 32. (Canceled)
- 33. (Currently Amended) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound selected from the group of compounds represented by Formula (I):

Goldstein et al.

Application No.: 10/045,903

Page 8

wherein:

R¹ is hydrogen or acyl;

R² is hydrogen or alkyl;

A is an aryl ring;

B is an aryl ring;

R³ is selected from the group consisting of:

- (a) acylamino;
- (b) optionally substituted heterocyclyl;
- (c) optionally substituted aryl or heteroaryl;
- (d) heteroalkenyl;
- (e) heteroalkynyl;
- (f) heteroalkoxy;
- (g) optionally substituted heterocyclylalkyl;
- (h) optionally substituted heterocyclylalkenyl;
- (i) optionally substituted heterocyclylalkynyl;
- (j) optionally substituted heterocyclylalkoxy, cyclyloxy, or heterocyclyloxy;
- (k) optionally substituted heterocyclylalkylamino;
- (l) optionally substituted heterocyclylalkylcarbonyl;
- (m) -NHSO₂R⁶ where R⁶ is optionally substituted heterocyclylalkyl;
- (n) -NHSO₂NR⁷R⁸ where R⁷ and R⁸ are, independently of each other, hydrogen, alkyl or heteroalkyl;

Goldstein et al.

Application No.: 10/045,903

Page 9

- Y is a single bond, -O-, -NH- or -S(O)_n- (where n is an integer from 0 to 2); and R⁹ is cyano, optionally substituted heteroaryl, -COOH, -COR¹⁰, -COOR¹¹, -CONR¹²R¹³, -SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHSO₂NR¹⁸R¹⁹, where R¹⁰ is optionally substituted heterocycle, R¹¹ is alkyl, and R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (p) $-C(=NR^{20})(NR^{21}R^{22})$ where R^{20} , R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are $(CH_2)_n$ where n is 2 or 3 and R^{22} is hydrogen or alkyl;
- (q) -NHC(=X)NR²³R²⁴ where X is O or S, and R²³ and R²⁴ are, independently of each other, hydrogen, alkyl or heteroalkyl;
- -CONR²⁵R²⁶ where R²⁵ and R²⁶ independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclylalkyl, or R²⁵ and R²⁶ together with the nitrogen to which they are attached form an optionally substituted heterocyclyl ring;
- (s) $-S(O)_nR^{27}$ where n is an integer from 0 to 2, and R^{27} is optionally substituted heterocyclylalkyl;
- (t) cycloalkylalkyl, cycloalkylalkynyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
- (u) arylaminoalkylene or heteroarylaminoalkylene;
- (v) Z-alkylene-NR³⁰R³¹ or Z-alkylene-OR³² where Z is -O-, and R³⁰,
 R³¹ and R³² are independently of each other, hydrogen, alkyl or
 heteroalkyl, wherein said alkylene and alkyl groups are
 optionally substituted with one to two groups selected from OH
 and O(alkyl);
- (w) -OC(O)-alkylene-CO₂H, <u>or</u> -OC(O)-NR'R", <u>or CO₂NHR'</u> (where R' and R" are independently hydrogen or alkyl); and

Application No.: 10/045,903

Page 10

(x) heteroarylalkenylene or heteroarylalkynylene;

R⁴ is selected from the group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) alkoxy; and
- (e) hydroxy;

R⁵ is selected from the group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) haloalkyl;
- (e) thioalkyl;
- (f) hydroxy;
- (g) amino;
- (h) alkylamino;
- (i) dialkylamino;
- (j) heteroalkyl;
- (k) optionally substituted heterocycle;
- (l) optionally substituted heterocyclylalkyl;
- (m) optionally substituted heterocyclylalkoxy;
- (n) alkylsulfonyl;
- (o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;
- (p) heteroalkoxy; and
- (q) carboxy;

R⁶ is selected from a group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl; and

Goldstein et al. PATENT

Application No.: 10/045,903

Page 11

(d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

34-37. (Canceled)

- 38. (Currently amended). The method of Claim 35 33 wherein the disease is rheumatoid arthritis.
- 39. (Previously Presented). The method of Claim 33 wherein the disease is adult respiratory distress syndrome.
- 40. (Previously Presented). The method of Claim 33 wherein the disease is asthma.
- 41. (Canceled)
- 42. (New) The method of claim 16, wherein R³ is optionally substituted heteroaryl selected from pyridinyl, N-oxidopyridinyl or pyridonyl.
- 43. (New) The method of claim 42, wherein R³ is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-4-yl or pyridon-2-yl, each of which may be optionally substituted
- 44. (New) The compound of claim 28, wherein Y is -O-alkylene and R⁹ is -COOH:
- 45. (New) The compound of claim 28, wherein R^3 is -(alkylene)- $SO_2NR^{34}R^{35}$ where R^{34} and R^{35} each independently is hydrogen or alkyl.